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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/679,705	10/05/2000	Jonathan Beckwith	HMV-052.01	8942

25181 7590 07/29/2002

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EXAMINER	
LOEB, BRONWEN	
ART UNIT	**PAPER NUMBER**
1636	14

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/679,705	Applicant(s) BECKWITH ET AL.	
	Examiner Bronwen M. Loeb	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2001 and 07 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50,55 and 56* is/are pending in the application.

4a) Of the above claim(s) *1-28 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-47,50,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *18 July 2001* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is in response to the amendment filed 18 July 2001 in which claims 26 and 45 were amended and the amendment filed 7 May 2002 in which claim 29 was amended, new claims 55 and 56 were presented and claims 51-54 were cancelled.

Claims 1-50, 55 and 56 are pending.

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 29-48, 50 and new claims 55 and 56, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that there is no undue burden to search all of the groups. This is not found persuasive because the searches of these two groups is not co-extensive. For instance, art that anticipates claim 1 would not necessarily anticipate claim 29. Thus, the search is burdensome.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-28 and 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Drawings

3. The corrected or substitute drawings were received on 18 July 2001. These drawings are acceptable.

Claim Objections

4. Claim 30, 32, 46 and 50 are objected to because of the following informalities: Claims 30, 32 and 46 use the phrase "wild type" as an adjective; in this use, it should be hyphenated. Claim 50 would be grammatically improved by amending it to recite "A method for producing a protein having at least one disulfide bond[,] comprising:". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 39-42 have been examined assuming that the modification to which they refer is the one to achieve increased proliferation.

7. Claims 29-42, 44-48 and 50 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the

invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 29 is drawn to a prokaryotic cell that is genetically modified to shift the redox status of the cytoplasm to a more oxidative state and another genetic modification to increase proliferation. This is a genus claim in terms of any genetic modification that increase the cell's ability to proliferate. The specification mentions a specific mutation in the ahpC. This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all genetic modifications that will increase the ability to proliferate based on the teachings in the specification. The single species disclosed in the specification was inadvertently identified (p. 42, Example 1) and characterized as a suppressor mutation. Further characterization shows it requires activity of the glutaredoxin system to be able to increase proliferation. The specification teaches that the genetic modification can involve mutation of a host cell gene or by the introduction of a gene into the host cell (pp. 12-13). The specification teaches how to screen for such genetic

modifications (pp. 18-20). However, the specification fails to teach any other specific examples of genetic modifications which increase proliferation. No other specific genes are suggested for mutation, suppressor or otherwise, or for heterologous expression to achieve the proliferation increase. For the single species disclosed, a specific mutation of the AhpC protein, there is no structure-function correlation taught indicating where other mutations to AhpC would yield the desired phenotype. There is no teaching of what amino acids are in the hydrophobic core of the protein, in the catalytic site or in the binding pocket which would demonstrate the Applicant knew where to make genetic modifications to reduce its peroxidase activity. While claim 42 recites the mutation is located in a region containing four triplet repeats, there is no discussion/evidence that any mutation in the region of any four triplet repeat in the ahpC coding sequence would yield the desired phenotype. Therefore, the specification does not describe the claimed genetic modifications to increase proliferation in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these genetic modifications at the time of filing the present application. Thus, the written description requirement has not been satisfied.

8. Claim 46 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the

invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 46 is drawn to a prokaryotic cell having a catalyst of disulfide bond formation and/or isomerization wherein the catalyst is a variant of a protein of the thioredoxin superfamily having a redox potential that is higher than that of its wild-type counterpart. This is a genus claim in terms of any variant in any protein of the thioredoxin superfamily that has a higher redox potential than its wild-type version. The specification mentions mutations in the –C-Xaa-Xaa-C- active site motif of most cysteine oxidoreductases (p. 23). This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the variants that will increase the redox potential of any of the thioredoxin superfamily proteins based on the teachings in the

specification. The specification teaches that variants may include amino acid substitutions, deletions or additions (p. 23, lines 12-13). There is no disclosure, other than of the active site motif –C-Xaa-Xaa-C-, of regions where substitutions, deletions or additions would yield increased redox potential. There is no overall structure-function correlation for all the proteins of the thioredoxin superfamily at all. Therefore, the specification does not describe the claimed variants of any protein in the thioredoxin superfamily having a higher redox potential in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these variants at the time of filing the present application. Thus, the written description requirement has not been satisfied.

9. Claims 55 and 56 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 55 is drawn to a prokaryotic cell having ATCC Accession No. PTA-938. Claim 56 is drawn to a prokaryotic cell having ATCC Accession No. PTA-939. The specification does not teach one how to make either of these specific prokaryotic cells thus one of skill in the art would not be able to make or use them. The specification also does not provide sufficient information about the biological deposit of either of these two cells; specifically the address of the depository is missing on p. 42, lines 37-39. A deposit of each of these cells in accordance with the information below would satisfy the enablement requirements of 35 U.S.C. §112.

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. See 37 CFR 1.801 through 1.809. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

10. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 29-48, 50, 55 and 56 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is vague and indefinite for three reasons. First it essentially recites two different genetic modifications; to clarify this, these should be referred to as a first and a second genetic modification. Second, the claim recites "a more oxidative state that favors disulfide bond formation". This renders the claim vague and indefinite as it is a relative phrase but it is unclear compare to what the cytoplasm has a more oxidative state. Third, the claim recites "contains a genetic modification that increases its ability to proliferate". Compared to what is the ability to proliferate increased, a cell without only this second genetic modification or one without either of the genetic modifications?

Claim 31 is vague and indefinite in reciting "reductase is selected from the group consisting of thioredoxin reductase, glutathione reductase and glutatione". "Glutathione" is not a reductase.

Claim 33 is vague and indefinite in reciting "reductase is selected from the group consisting of thioredoxin reductase, glutathione reductase and glutatione". "Glutathione" is not a reductase.

Claim 39 is vague and indefinite in reciting "the genetic modification". To which of the two genetic modifications recited in parent claim 29 does this refer?

Claim 40 is vague and indefinite in reciting "the modification". To which of the two genetic modifications recited in parent claim 29 does this refer?

Claim 40 is vague and indefinite in reciting "restores at least some of the reducing capacity". Compared to what is the reducing capacity restored?

Claim 41 is vague and indefinite in reciting "the modification". To which of the two genetic modifications recited in parent claim 29 does this refer?

Claim 43 recites the limitation "the mutated ahpC protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 50 recites the limitation "a host cell of claim 29" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

Claims 29-48, 50, 55 and 56 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 10:00 AM to 6:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Tracey Johnson, Patent Analyst whose telephone number is (703) 305-2982.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

July 27, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

09/679,705

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date	
07 May 2002	26 April 2002	Papers #13 + 12

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

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If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 14